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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.	
09/734,460	12/11/2000	Jerome B. Zeldis	9516-018 5112		
20583	7590 11/20/2002				
	ID EDMONDS	EXAMINER			
	JE OF THE AMERICA , NY 100362711	AS	EVANS, CH	HARESSE L	
			ART UNIT	PAPER NUMBER	
			1615	Φ-	
			DATE MAILED: 11/20/2002	HO	

Please find below and/or attached an Office communication concerning this application or proceeding.

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,		Application No.		Applicant(s)				
Office Action Summary		09/734,460		ZELDIS, JEROME	B.			
		Examiner		Art Unit				
		Charesse L. Eva		1615				
The MAILING DATE of this communication appears on the cover sheet with the correspondence address Period for Reply								
THE MAILING DATE O  - Extensions of time may be ava after SIX (6) MONTHS from the f the period for reply specified f NO period for reply is specified Failure to reply within the set o	JTORY PERIOD FOR REPLY F THIS COMMUNICATION.  iilable under the provisions of 37 CFR 1.13 e mailing date of this communication.  above is less than thirty (30) days, a reply ed above, the maximum statutory period w r extended period for reply will, by statute, e later than three months after the mailing . See 37 CFR 1.704(b).	36(a). In no event, how y within the statutory m will apply and will expire , cause the application	vever, may a reply be tim inimum of thirty (30) day: SIX (6) MONTHS from to become ABANDONE	nely filed s will be considered timely, the mailing date of this cord (35 U.S.C. § 133).	mmunication.			
1) Responsive to c	ommunication(s) filed on 22 A	<u> August 2002</u> .						
2a)☐ This action is FII	NAL. 2b)⊠ Th	is action is non-	final.					
	ation is in condition for allowa ance with the practice under				e merits is			
4)⊠ Claim(s) <u>1-42</u> is/	4)⊠ Claim(s) <u>1-42</u> is/are pending in the application.							
4a) Of the above	4a) Of the above claim(s) <u>3,6,19 and 32-42</u> is/are withdrawn from consideration.							
5) Claim(s) is								
6)⊠ Claim(s) <u>1,2,4,5,7</u>	6)⊠ Claim(s) <u>1,2,4,5,7-10,12-18 and 20-23</u> is/are rejected.							
7)⊠ Claim(s) <u>11 and 2</u>	24-31 is/are objected to.							
. ,	re subject to restriction and/or	r election require	ement.					
Application Papers								
<u> </u>	s objected to by the Examine							
	ed on is/are: a)□ accep	-	-					
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).								
11) The proposed drawing correction filed on is: a) approved b) disapproved by the Examiner.								
If approved, corrected drawings are required in reply to this Office action.  12)☐ The oath or declaration is objected to by the Examiner.								
Priority under 35 U.S.C. §§ 119 and 120								
<u></u>	is made of a claim for foreign	n priority under 3	5 I I S C & 119(a	)-(d) or (f)				
a) ☐ All b) ☐ Some		r priority under o	5 6.6.6. 3 115(a	)-(d) 01 (l).				
<u> </u>	ppies of the priority documents	s have been rec	eived					
	•			on No				
3.☐ Copies of the applica								
	14)⊠ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).							
a) ☐ The translation of the foreign language provisional application has been received.  15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.								
Attachment(s)		• • • • • • • • • • • • • • • • • • • •						
Notice of References Cited     Notice of Draftsperson's Pal     Information Disclosure State		4) 5) 6)	Notice of Informal F	(PTO-413) Paper No(s Patent Application (PTO				

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#### **DETAILED ACTION**

### Priority

Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged.

# Action Summary

Acknowledgement is made of the receipt of the Response to Restriction Requirement wherein applicant, elected, with traverse, 1-oxo-2-(2,6-dioxopiperidin-3-yl)-4-amino-isoindoline. Applicant has reserved the right to prosecute the non-elected subject matter in one or more subsequent divisional or continuing application(s).

Claim 19 has not been considered as it does not read on applicant's species election which includes claims 1, 2, 4, 5, 7-18 and 20-31. Claim 19 should be included in the non-elected subject matter.

Claims 1, 2, 4, 5, 7-18 and 20-31 are active in this Action.

# Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

<sup>(</sup>a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary

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skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2, 4, 5, 7-10, 12-18, 20-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Muller et al (US 5,635,517). The claims are directed to a methods of preventing atheroschelerosis and stenosis in a mammal comprising administering an effective amount of a TNF-alpha inhibitor, such as 1-oxo-2-(2,6-dioxopiperidin-3yl)-4-aminoisoindoline.

Muller teaches a class of compounds used to decrease the levels of TNF-alpha. Specific compounds falling within the disclosed formula include 1-oxo-2-(2,6-dioxopiperidin-3-yl)-4-aminoisoindoline (column 7, lines 12). The referenced compounds are used to inhibit the undesirable effects of TNF-alpha and can be administered orally, rectally, or parenterally, alone or in combination with other therapeutic agents (column 4, lines 36-40). Oral dosage forms include tablets, capsules, dragees and similar shaped compressed pharmaceutical forms containing from 1 to 100mg of drug per unit dosage (column 6, lines 35-37). Please refer to Example 5 for an illustration of a preparation of tablets for chewing (column 9, Example 5). While the reference does not expressly teach applicant's claimed amounts, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. Where the general conditions of a claim are disclosed in the

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prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. *In re Aller*, 220 F.2d 454, 105 USPQ 233, 235 (CCPA 1955). It is the position of the examiner that these are limitations that would be routinely determined by one of ordinary skill in the art, through minimal experimentation, as being suitable, absent the presentation of some unusual and/or unexpected results. Absent a clear showing of criticality, the determination of the particular ranges and administration regiment is within the skill of the ordinary worker as part of the process of normal optimization. The courts have held the "concentration limitations are obvious absent a showing of criticality." <u>Azko v. E.E. Pont de Nemours</u>, 1 USPQ 2d 1704 (Fed. Cir. 1987).

The cited reference does not expressly teach utilizing this compound for the prevention of atherosclerosis or restenosis. However, it does teach a method of reducing tumor necrosis factor-alpha (TNF-alpha) levels with this compound.

Excessive or unregulated TNF-alpha production has been implicated in a number of disease states. Therefore, decreasing TNF-alpha levels constitutes a valuable therapeutic strategy for the treatment of these inflammatory, infectious, immunological or malignant diseases such as congestive heart failure (column 3, lines 59-65). Congestive heart failure is related to the group of ischemic heart diseases that also include atherosclerosis and coronary artery disease. Accordingly, it would have been obvious to one of ordinary skill in the art at the time of the invention to modify

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the reference of Muller by formulating a pharmaceutical regimen that would decrease or mitigate factors that are known to cause damage and impairment to the muscle fibers that relate to the contractility of the heart muscle.

## Claim Objections

Claim 10 is objected to because of the following informalities: claim 10 refers to claims "...1, 2, 3" at the same time rather than only referring to only one claim at a time. Appropriate correction is required.

Claims 11 and 24-31 are objected to as being dependent upon a rejected base claim.

### Conclusion

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charesse L. Evans whose telephone number is 703-308-6400. The examiner can normally be reached on Monday-Thursday 7:00a - 4:30p; Alternating Fridays 7:00a - 3:30p.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on 703-308-2927. The fax phone

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numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

Charesse Evans November 15, 2002

THURMAN K. PAGE
SUPERVISORY PAYENT EXAMINER
TECHNOLOGY CENTER 1600